Facilitation of Resuscitation Device Development: An FDA Division of Cardiovascular Devices Perspective

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1. Medical Device Development Landscape
2. Next Steps
Medical Device Landscape

U.S. Medical Device Manufacturing Companies by Number of Employees

- < 10 employees: 69%
- < 20 employees: 10%
- < 100 employees: 14%
- < 200 employees: 5%
- < 1000 employees: 2%

Source: Dun and Bradstreet, Inc.
PMA

- Higher risk devices
- Establish **reasonable** assurance of **safety** and **effectiveness** using **valid scientific evidence**
- Bench - Animal - Human
- Similar to new drug approval process
1. Pre-clinical Testing
   - Are bench and animal studies acceptable?

2. Pivotal Trial
   - Design: Minimize bias and confounding
   - Execution: Minimize amount of missing data
   - Analysis: Rule out chance (i.e., several prospectively chosen, clinically relevant hypotheses with plan for alpha allocation)
   - Have clinically meaningful results been clearly demonstrated?

3. Manufacturing
   Can device be built safely for commercial distribution?

4. Is the Device Label truthful and accurate?
The Total Product Life Cycle and Device Regulation
Striking the Right Balance Between Pre- and Postmarket Evaluation

- Use appropriate amount of pre-market data to make primary decisions about approvability of new devices (safety, effectiveness)
- Use postmarket data to
  - supplement our understanding about device and operator performance
  - identify device malfunctions and take corrective action as necessary
  - modify pre-market expectations for next generation devices.
II. Next Steps
CDRH Strategic Priorities – Addressing Regulatory Uncertainty

2014 - 2015 Strategic Priorities

Center for Devices and Radiological Health

U.S. Food and Drug Administration
U.S. Department of Health and Human Services

CDRH 2014 Strategic Priorities; fda.gov website
CDRH Strategic Priorities

1. Strengthen Clinical Trial Enterprise
2. Strike the Right Balance Between Premarket and Postmarket Data Collection
3. Provide Excellent Customer Service
Improving the IDE process

- Early interaction with FDA is a key to addressing and resolving issues

- Need to address FDA concerns that are raised in Pre-IDE discussions

- Sufficient safety evidence is needed to begin clinical studies in U.S. – most disapprovals based on inadequate bench and/or animal testing
Key Principle for Approval of an Early Feasibility Study

- For some new devices, exhaustive nonclinical testing would not likely provide the information needed to further device development.

- In these cases, early clinical use of the device in a limited number of subjects is needed to:
  - provide initial insights into clinical safety and device function;
  - inform subsequent clinical and non-clinical testing; and/or
  - improve device performance through iteration before finalizing the design.

- Therefore, approval of an early feasibility study IDE may be based on less nonclinical data.

An EFS must be justified by an appropriate benefit/risk analysis, including justification for the types and amount of data need to support study initiation.
Words Into Deeds: Adherence to Benefit/risk principles is key

A core principle is the application of benefit/risk principles throughout all phases of medical device development.

Benefit/Risk Guidance
- Identifies the principle factors that can be used in making benefit/risk determinations during premarket review.
Streamlining Clinical Trials: US Clinical Trial Ecosystem Under Stress

- Risk averse environment: patients and hospitals
- Weak clinical study infrastructure
  - Contracting
  - Inexperienced sponsors, sites, and investigators
- Financial challenges
  - High cost of studies
  - Reimbursement delays or non-coverage
- Delays in study initiation
  - Regulatory requirements
  - IRB approval
- Enrollment challenges
  - Restrictive selection criteria
  - Competing studies
- Excessive time needed to complete studies
Understand FDA CDRH expectations

Interact early and appropriately with FDA CDRH

Encourage innovative trial design with caveat of prospective planning –

a. Combine proof of principle and proof of device trials when feasible

b. Optimize alignment with NIH review process (parallel)

c. Use sample size re-estimation techniques and other adaptive strategies when appropriate

Simultaneously assess and appropriately repair the entire clinical trials ecosystem